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STATEMENT OF ACCURACY OF TRANSLATION

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states that:

- (1) I am fully conversant both with the Japanese and English languages.
- (2) (A) I have translated into English, Japanese Patent Application Number _____, filed _____. A copy of said English translation is attached hereto.
- (2) (B) I have carefully compared the attached English-language translation of Japanese Patent Application Number 2005-038474 filed on February 15, 2005 with the original Japanese-language patent application.
- (3) The translation is, to the best of my knowledge and belief, an accurate translation from the original into the English language.

Date: February 12, 2010



Atsushi ITOH

(translation)

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[List of Attached Documents]	
[Name of Document]	Claims 1
[Name of Document]	Specification 1
[Name of Document]	Drawing 1
[Name of Document]	Abstract 1

CLAIMS

1. A hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion.

2. The hollow microparticle according to Claim 1, wherein the density of
5 chains composing the polymer brush layer is 0.4 to 1.2 chains/nm².

3. The hollow microparticle according to Claim 1, wherein the polymer chain composing the polymer brush layer is a block copolymer of at least one crosslinkable monomer and a non-crosslinkable monomer,

10 blocks of the crosslinkable monomer are located innermost of the polymer brush layer.

4. The hollow microparticle according to Claim 3, wherein the crosslinkable monomer is an oxetane acrylate or an oxetane methacrylate, and the non-crosslinkable monomer is selected from the group consisting of an acrylate derivative, a methacrylate derivative, a styrene derivative, vinyl acetate and
15 acrylonitrile.

5. The hollow microparticle according to Claim 2, wherein the molecular weight distribution index of each block of the polymer chain is from 1 to 1.50.

6. The hollow microparticle according to Claim 3, wherein the degree of polymerization of the crosslinkable monomer block is from 10 to 10000, and the
20 degree of polymerization of the non-crosslinkable monomer block is from 10 to 10000.

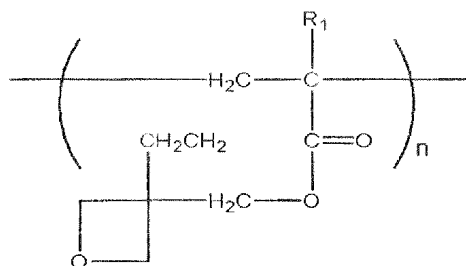
7. The hollow microparticle according to Claim 1, which has a particle size of from 60 nm to 5 μm.

8. A hollow microparticle comprising a hollow portion and a high-density
25 polymer brush layer enclosing the hollow portion, wherein a polymer chain composing the polymer brush layer is a block copolymer of:

i) a crosslinkable monomer block located at inner part of the polymer brush

layer, which is represented by the formula:

[Formula 1]

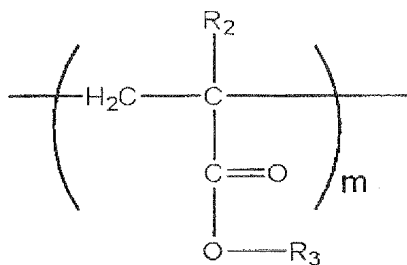


wherein

5 R_1 is a hydrogen atom or a C_1 to C_6 alkyl group, and n is from 10 to 10000; and

ii) a non-crosslinkable monomer block located at outer part of the polymer brush layer, which is represented by the formula:

[Formula 2]



10 wherein

R_2 is a hydrogen atom or a C_1 to C_6 alkyl group,

R_3 is a hydrogen atom, a C_1 to C_{12} alkyl group or a phenyl group, and

m is from 10 to 10000;

9. A process for producing a hollow microparticle comprising a hollow
15 portion and a high-density polymer brush layer enclosing the hollow portion,
comprising the steps of:

- a) attaching a polymerization initiation group to a microparticle surface;
- b) bringing into contact a microparticle having the polymerization initiation group on its surface with a crosslinkable monomer under the conditions for living

radical polymerization to obtain a composite microparticle in which a high-density polymer brush layer is attached to the microparticle surface;

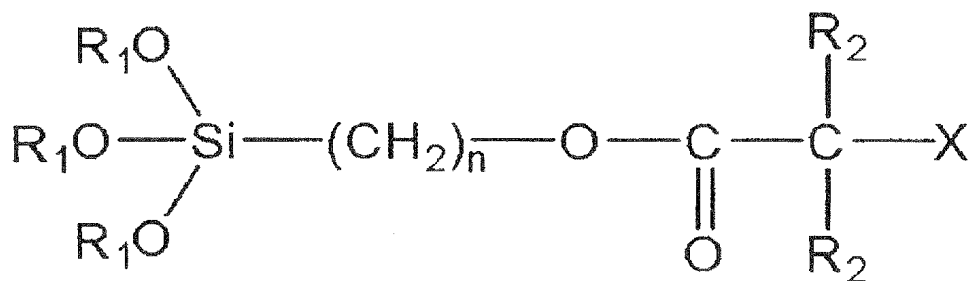
c) bringing into contact a crosslinkable polymer brush of the composite microparticle with a non-crosslinkable monomer under the conditions for living radical polymerization to obtain a composite microparticle in which a block copolymer is attached to the microparticle surface;

d) subjecting the composite microparticle in which the block copolymer is attached to the microparticle surface to the conditions for crosslinking reaction; and

e) bringing into contact the composite microparticle in which the block copolymer is attached to the microparticle surface with an eluent under such conditions that the microparticle is only eluted with no influence on the block copolymer to elute only the microparticle.

10. The process according to Claim 9, wherein the step a) is carried out by bringing into contact a compound represented by the formula:

[Formula 3]



wherein

n is an integer of from 3 to 10,

R₁ represents a C₁ to C₃ alkyl,

R₂ represents a C₁ to C₂ alkyl, and

X represents a halogen atom,

with a microparticle of silica, a metal oxide or a metal sulfide under such conditions that the compound and the microparticle may react.

11. The process according to Claim 9, wherein the crosslinkable monomer is an oxetane acrylate or an oxetane methacrylate, and

the non-crosslinkable monomer is selected from the group consisting of an acrylate derivative, a methacrylate derivative, a styrene derivative, vinyl acetate and acrylonitrile.

12. The process according to Claim 9, wherein the eluent is an aqueous solution of hydrogen fluoride.

DESCRIPTION

High-Density Polymer Brush-Coated Hollow Microparticles, Processes for
Producing the Same and Applications of High-Density Polymer Brush-Coated
Hollow Microparticles

5 TECHNICAL FIELD

The present invention relates to a hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion and a process for producing the same. In addition, the present invention relates to a method for controlling alignment thereof and applications thereof.

10 BACKGROUND ART

Microparticle polymers have shapes which can provide characteristics such as spherization (monodispersing), heteromorphization, porosity (hollowing), complexing, impartment of surface reactivity and so on and are, therefore, used in a wide variety of fields, such as in additives for cosmetics, carrier particles for
15 diagnostic reagents, pharmacy and medicine, information-displaying materials such as liquid crystal spacers, additives for plastics and the like, taking advantage of their submicron sizes.

Hollow polymer microparticles have conventionally been produced by such a process as incorporating a blowing agent in resin particles and then allowing the
20 blowing agent to expand, encapsulating a volatile material in a polymer and then allowing the volatile material to vaporize and expand, or melting a polymer and injecting a gas such as air into the polymer.

By means of such processes, however, it has been difficult to produce predetermined hollow particles in a steady manner. On the other hand, Patent
25 Reference 1 discloses a process for producing hollow particles which comprises preparing a dispersion of monomer components comprising hydrophilic, crosslinkable and/or other monomers coexistent with an oily component,

polymerizing the monomers to obtain resin particles and then removing the oily component to provide hollow particles. The mere preparation of a dispersion of monomers and an oily component, however, has a disadvantage that control of hollow structure is highly difficult and inefficient.

5 In order to solve such a problem, further studies have been conducted for processes for producing hollow microparticles, and processes have been proposed, such as layer-by-layer technique and a process which comprises utilizing copolymerization of divinyl monomers and the like, coating surfaces of microparticles as templates with an organic or inorganic substance and then
10 removing the template microparticles to provide hollow microparticles. Controllability of hollow structures has been improved to some extent, while at least one of the improvement in productivity, the improvement in dispersibility of microparticles and the impartment of functions to microparticles is still insufficient, leaving a number of problems to be addressed.

15 In addition, Patent Reference 2 discloses hollow macromolecular microparticles in which shells are formed of a crosslinkable polymer and a process for producing the same. According to this process, hollow macromolecular microparticles having a high porosity can be obtained. There is, however, a disadvantage that the shells are so thin that the particles can not be used in
20 applications where their strength is required and nothing of methods for controlling particle strength or for orderly aligning the particles has been disclosed.

Just for reference, the inventors have succeeded in production of a brush-form, high-density polymer particle in which grafted chains extend in a vertical direction from the surface of the particle, by attaching a crosslinkable polymer to the surface
25 of an inorganic particle (SiO_2) through graft polymerization and then performing living radical polymerization and have filed an application (Patent Reference 3). Such composite microparticles made of high-density grafted chains attached to

microparticle surfaces can perform alignment control of the microparticles driven by steric repulsion by high-density grafted chains to form colloidal crystals.

Patent literature 1: Japanese Laid-Open Patent Publication No. 1993-125127

Patent literature 2: Japanese Laid-Open Patent Publication No. 2004-190038

5 Patent literature 3: Japanese Patent Application No. 2004-139213

DISCLOSURE OF THE INVENTION

PROBLEMS TO BE SOLVED BY THE INVENTION

The present invention is intended to provide a process for hollowing a composite microparticle made of high-density grafted chains attached to a
10 microparticle surface without compromising characteristics of prior art, high-density polymer particles of having a narrow particle size distribution and an excellent dispersion stability and to provide, by such a process, a hollow microparticle comprising a high-density polymer brush layer and a hollow portion.

MEANS FOR SOLVING THE PROBLEMS

15 After conducting a keen examination, the inventors have confirmed that it is possible to obtain a hollow microparticle, by eluting only a microparticle from a composite microparticle made of high-density grafted chains attached to a microparticle surface to hollow the composite microparticle, while retaining characteristics of prior art, high-density polymer particles, to successfully solve the
20 above problems.

Therefore, the present invention provides the following.

(1) A hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion.

(2) The hollow microparticle according to (1) wherein the density of chains
25 composing the polymer brush layer is from 0.4 to 1.2 chains/nm².

(3) The hollow microparticle according to (1) or (2) wherein the polymer chain composing the polymer brush layer is a block copolymer of at least one

crosslinkable monomer and a non-crosslinkable monomer,

blocks of the crosslinkable monomer are located innermost of the polymer brush layer,.

(4) The hollow microparticle according to any one of (1) to (3) wherein the
5 crosslinkable monomer in the polymer chain composing the polymer brush layer is
an oxetane acrylate or an oxetane methacrylate, and

the non-crosslinkable monomer is selected from the group consisting of an
acrylate derivative, a methacrylate derivative, a styrene derivative, vinyl acetate and
acrylonitrile.

10 (5) The hollow microparticle according to any one of (1) to (4) wherein the
molecular weight distribution index of each block of the polymer chain composing
the polymer brush layer is from 1 to 1.50.

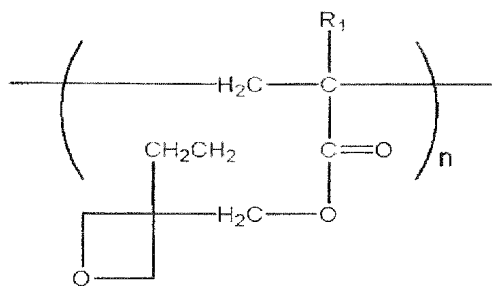
(6) The hollow microparticle according to any one of (1) to (5) wherein the
degree of polymerization of the crosslinkable monomer block in the polymer chain
15 composing the polymer brush layer is from 10 to 10000, and the degree of
polymerization of the non-crosslinkable monomer block in the polymer chain
composing the polymer brush layer is from 10 to 10000.

(7) The hollow microparticle according to any one of (1) to (6) which has a
particle size of from 60 nm to 5 μ m.

20 (8) A hollow microparticle comprising a hollow portion and a high-density
polymer brush layer enclosing the hollow portion, wherein a polymer chain
composing the polymer brush layer is a block copolymer of:

i) a crosslinkable monomer block located at inner part of the polymer brush
layer, which is represented by the formula:

25 [Formula 4]



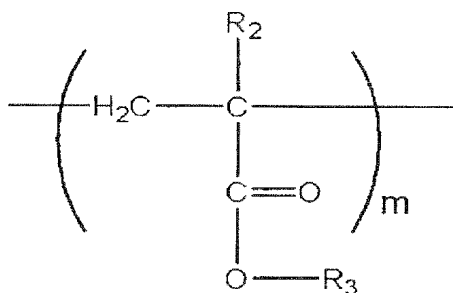
wherein

R_1 is a hydrogen atom or a C_1 to C_6 alkyl group, and n is from 10 to 10000; and

ii) a non-crosslinkable monomer block located at outer part of the polymer

5 brush layer, which is represented by the formula:

[Formula 5]



wherein

R_2 is a hydrogen atom or a C_1 to C_6 alkyl group,

10 R_3 is a hydrogen atom, a C_1 to C_{12} alkyl group or a phenyl group, and

m is from 10 to 10000.

(9) The hollow microparticle according to (8), wherein the chain density of the polymer chain composing the polymer brush layer is 0.4-1.2 chains/nm²..

(10) The hollow microparticle according to (8) or (9), wherein the molecular
15 weight distribution index of each block of the polymer chain composing the polymer brush layer is from 1 to 1.50.

(11) The hollow microparticle according to any one of (8) to (10), which has a particle size of from 60 nm to 5 μ m.

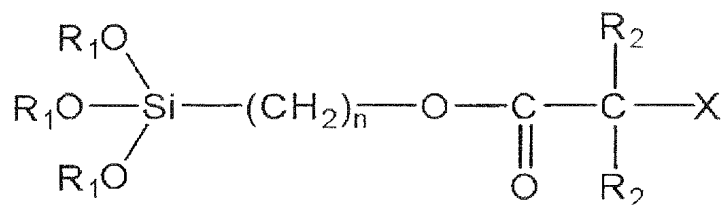
(12) A process for producing a hollow microparticle comprising a hollow

portion and a high-density polymer brush layer enclosing the hollow portion,
comprising the steps of:

- a) attaching a polymerization initiation group to a microparticle surface;
- b) bringing into contact a microparticle having the polymerization initiation
5 group on its surface with a crosslinkable monomer under the conditions for living
radical polymerization to obtain a composite microparticle in which a high-density
polymer brush layer is attached to the microparticle surface;
- c) bringing into contact a crosslinkable polymer brush of the composite
microparticle with a non-crosslinkable monomer under the conditions for living
10 radical polymerization to obtain a composite microparticle in which a block
copolymer is attached to the microparticle surface;
- d) subjecting the composite microparticle in which the block copolymer is
attached to the microparticle surface to the conditions for crosslinking reaction; and
- e) bringing into contact the composite microparticle in which the block
15 copolymer is attached to the microparticle surface with an eluent under such
conditions that the microparticle is only eluted with no influence on the block
copolymer to elute only the microparticle.

(13) The process according to (12) wherein the step a) is carried out by
bringing into contact a compound represented by the formula:

20 [Formula 6]



wherein

n is an integer of from 3 to 10,

R₁ represents a C₁ to C₃ alkyl,

R₂ represents a C1 to C2 alkyl, and

X represents a halogen atom,

with a microparticle of silica, a metal oxide or a metal sulfide under such conditions that the compound and the microparticle may react.

5 (14) The process according to (12) wherein the crosslinkable monomer is an oxetane acrylate or an oxetane methacrylate, and

the non-crosslinkable monomer is selected from the group consisting of an acrylate derivative, a methacrylate derivative, a styrene derivative, vinyl acetate and acrylonitrile.

10 (15) The process according to (12) wherein the eluent is an aqueous solution of hydrogen fluoride.

EFFECT OF THE INVENTION

According to the processes for producing a hollow microparticle of the present invention, a hollow particle, while retaining characteristics of prior art, high-density
15 polymer particles of having a narrow particle size distribution and an excellent dispersion stability, can be obtained.

In addition, any hollow particles may be obtained by the selection of particle shape and size. Further, shape-retaining characteristics (rigid or flexible) of the hollow portion may be controlled by adjusting the degree of polymerization and the
20 like of the crosslinkable polymer for the inner layer, and a sustained release rate and/or intake rate can also be controlled when the hollow portion is to carry or take in a reagent and agent.

Moreover, particle sizes can arbitrarily be designed by controlling the film thickness of the outer, high-density grafted chains.

25 BEST MODE FOR CARRING OUT THE INVENTION

The present invention is now described. It is to be understood that throughout this specification, expressions in singular forms, “a”, “an” and “the” also include

plural concepts thereof unless otherwise specified. It is also to be understood that all scientific and technical terms used in this specification have meanings commonly used in the art unless otherwise specified.

(Terms)

5 Terms used specifically in this specification will now be enumerated with respect to their definitions.

The term “hollow microparticle” used herein means a structure composed of a hollow portion to be defined below and a high-density polymer brush layer enclosing the hollow portion.

10 The term “high-density” used herein means a macromolecular chain density at an incomparably higher level, which is a density of grafted chains when such macromolecular chains are so dense that steric repulsion may occur between the macromolecular chains. In such a case, the macromolecular chains assume a form stretched nearly to the full extent in a direction perpendicular to the surface. For
15 example, assuming that polymethyl methacrylate chains as grafted chains were stretched straight to the full extent in a direction perpendicular to the surface, a density of 0.4 chains/nm² or more would be attained.

The term “polymer chain” used herein means a chain of two or more molecules, formed by polymerization reaction, stretching from a microparticle surface, and can
20 be used interchangeably with “macromolecular chain” or “macromolecular grafted chain.”

The term “chain density” or “density” used herein means a number of macromolecular chains aligned per unit area (nm²) on a surface.

The term “polymer brush layer” used herein means a structure in which
25 individual macromolecular chains in a high density are oriented and aligned in relation to the surface of a “microparticle” or “hollow portion” to be defined below and in which a macromolecular chain is crosslinked with another macromolecular

chain (see Fig. 1, for example). A “macromolecular chain” used here may be a homopolymer of crosslinkable monomers or a copolymer of a crosslinkable monomer and a non-crosslinkable monomer.

The term “crosslinking” used herein means a state in which adjacent
5 macromolecular chains are linked by a chemical reaction between the macromolecular chains to a degree such that individual macromolecules may not disintegrate in eluting only a microparticle from a composite microparticle in which a polymer brush layer is attached to the surface.

The term “crosslinkable monomer” used herein means a monomer having, in
10 addition to polymerizable groups, crosslinkable functional groups in its side chain. On the other hand, a polymer in which polymerizable groups contained in crosslinkable monomers have been polymerized and crosslinkable functional groups remain unreacted is referred to as a “crosslinkable polymer.”

The term “crosslinkable monomer block” used herein means a polymer block
15 made of polymerized crosslinkable monomers.

The term “non-crosslinkable monomer” used herein means a monomer having polymerizable groups and absolutely no crosslinkable functional groups. On the other hand, a polymer of non-crosslinkable monomers is referred to as a “non-crosslinkable polymer.”

20 The term “non-crosslinkable monomer block” used herein means a polymer block made of polymerized non-crosslinkable monomers.

The term “hollow portion” used herein means a space enclosed by a polymer brush layer in a hollow microparticle as defined above, into which artificial or biological substances, singly or in combination, capable of being in the form of a gas,
25 liquid (solution, dispersion, etc.), gel, semi-solid or solid may be filled.

The term “microparticle” used herein means a bare microparticle before a polymer brush layer as defined above is attached to its surface, and may be used in

distinction from a “hollow microparticle” as defined above. Any solid particle with a particle size of from 50 nm to 1 μ m, being monodispersed and capable of being eluted by an eluent which will not adversely affect (degrade, break, etc.) the polymer brush layer, but not limited, may be inorganic substances or organic substances..

5 The term “composite microparticle” used herein means a microparticle formed of a “polymer brush layer” as defined above attached to a microparticle surface, and is used herein in distinction from a “microparticle” and “hollow microparticle” as defined above.

The term “living radical polymerization” used herein means a polymerization
10 such that, for a polymerization reaction with no or negligible chain transfer or termination reaction, the produced polymer will retain polymerization activity at the terminus even after the termination of the reaction so that a polymerization reaction may be reinitiated upon addition of monomers. Characteristics of living radical polymerization include a capability of synthesizing polymers having any average
15 molecular weights by adjusting the concentration ratio between monomers and a polymerization initiator, an extremely narrow distribution of molecular weights of produced polymers and applicability to block copolymers. Living radical polymerization is herein abbreviated as “LRP.” In addition, examples of monomers capable of radical polymerization for composing grafted chains include MMA
20 (methyl methacrylate), styrene and vinyl acetate.

The term “under the conditions for living radical polymerization” used herein means to adopt polymerization conditions as appropriately selected by those skilled in the art such that living radical polymerization may surely and well proceed on the basis of polymerization initiation group provided on the surfaces of microparticles.

25 The term “polymerization initiation group” used herein means a substance which is added in a small amount to monomers to function as an initiator of a polymerization reaction, and any substances may be used without limitation as long

as such function is provided.

The term “hollowing” or “hollowing treatment” used herein means a process for removing (for example, eluting or liquating) only a microparticle from a composite microparticle in which a polymer brush layer is attached to a microparticle surface, without adversely affecting the polymer brush layer.

(Description of Preferred Embodiment)

Preferred embodiments of the present invention will be described below. It is to be understood that the embodiments to be presented below are provided for better understanding of the invention and that the scope of the invention should not be limited to the description below. It is, therefore, obvious that those skilled in the art may make modifications to the invention within the scope thereof in the light of the description herein.

In one aspect, the present invention provides a hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion. Thus, the hollow microparticle includes the high-density polymer brush layer having a structure in which individual macromolecular chains are oriented and aligned in a high density in relation to the surface of the hollow portion and in which crosslinkable functional groups contained in a macromolecular chain is crosslinked with other crosslinkable functional groups of another macromolecular chain, therefore, providing an advantage of having a much higher particle strength in comparison to conventional hollow microparticles not having such a polymer brush structure.

The density of polymer chains composing the polymer brush layer is preferably from 0.4 to 1.2 chains/nm². When the density of polymer chains is below 0.4 chains/nm², the brush structure will be sparse, not allowing steric repulsion to occur between adjacent macromolecular chains, with a disadvantage that the chains can not assume a fully stretched form and the particle strength will decrease. In addition, it

is unfavorable for application for carrying or taking in reagents or agents into the hollow portion. Also, when the density of polymer chains is above 1.2 chains/nm², the chain density will be so high that the hollow particle may have a poor stability.

In one preferable embodiment, the polymer chain composing the polymer
5 brush layer is a block copolymer of at least one crosslinkable monomer and a non-crosslinkable monomer and blocks of the crosslinkable monomer are located innermost of the polymer brush layer. Thus, the inner layer serving as a scaffolding for the polymer brush layer is reinforced by the crosslinking reaction as described above (see Fig. 1, for example) so that the whole polymer brush layer may be
10 stabilized. Additionally, according to the present invention, by adjusting the degree of crosslinking and the like of the crosslinkable polymer for the inner layer, shape-retaining characteristics (rigid or flexible) of the hollow portion may advantageously be controlled. Also, when the hollow portion is to carry or take in a reagent and agent, their sustained release rate and/or intake rate can also be controlled.
15 Furthermore, particle sizes can arbitrarily be designed by controlling the film thickness of the non-crosslinkable polymer of the outer layer.

Crosslinkable monomers preferred for use in the present invention include, but not limited to, an oxetane acrylate or an oxetane methacrylate and a monomer so long as the monomer has a crosslinkable portion by light, heat or a polymerization
20 initiator in addition to a living radical polymerizable group in the side chain.. Non-crosslinkable monomers preferred for use in the present invention include, but not limited to, an acrylate derivative, a methacrylate derivative, a styrene derivative, vinyl acetate and acrylonitrile.

Hollow microparticles can be synthesized relatively easily using any of the
25 crosslinkable monomers and non-crosslinkable monomers mentioned above, with an advantage of being suitable for industrial mass production.

The molecular weight distribution index of each block of a polymer chain in a

hollow microparticle according to the present invention is preferably from 1 to 1.50, and more preferably from 1 to 1.30. Such ideal or nearly ideal monodispersed hollow microparticles can easily be obtained by the process for producing hollow microparticles according to the present invention.

5 The degree of polymerization of the crosslinkable monomer block composing the polymer brush layer of the hollow microparticle according to the present invention is preferably from 10 to 10000, and more preferably from 100 to 5000. The degree of polymerization of the non-crosslinkable monomer block is preferably from 10 to 10000, and more preferably from 100 to 5000.

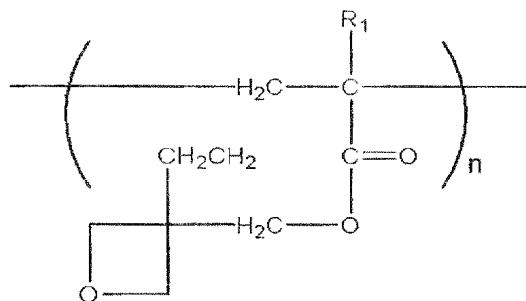
10 According to the process for producing hollow microparticles of the present invention, within the range of a particle size of from 60 nm to 5 μm , the particle size of a hollow microparticle, the film thickness of the polymer brush layer and the chain density of polymer chains can freely be controlled.

Also, as an initial stage of production of hollow microparticles, in order to graft
15 polymerize at a high density from the surface of a microparticle as a template, the particle size of the microparticle is preferably from 50 nm to 1 μm . If the particle size of the microparticle was below 50 nm, the curvature of the particle would have an influence in the graft polymerization from the microparticle surface, lowering the density of macromolecular chains at the polymer brush layer. If the particle size of
20 the microparticle was above 1 μm , dispersion of composite microparticles or hollow microparticles in a solvent would unfavorably be difficult.

In the most preferred embodiment, the present invention provides a hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion, wherein a polymer chain composing the polymer brush
25 layer is a block copolymer of:

i) a crosslinkable monomer block located at inner part of the polymer brush layer, which is represented by the formula:

[Formula 7]

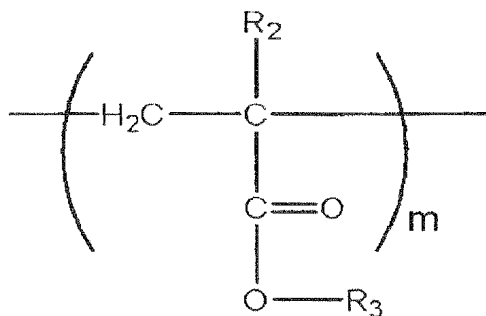


wherein

R_1 is a hydrogen atom or a C_1 to C_6 alkyl group, and more preferably a hydrogen atom or a methyl group, n is from 10 to 10000; and

ii) a non-crosslinkable monomer block located at outer part of the polymer brush layer, which is represented by the formula:

[Formula 8]



10 wherein

R_2 is a hydrogen atom or a C_1 to C_6 alkyl group, and more preferably a hydrogen atom or a methyl group,

R_3 is a hydrogen atom, a C_1 to C_{12} alkyl group or a phenyl group, and more preferably a hydrogen atom, a C_1 to C_3 alkyl group or a phenyl group, and m is from 10 to 10000.

The term "alkyl group" used herein refers to a monovalent group produced from an aliphatic hydrocarbon such as methane, ethane and propane (alkanes) which is deprived of one hydrogen atom, generally represented by $C_nH_{2n}-$ wherein n is a

positive integer. An alkyl group can be straight or branched.

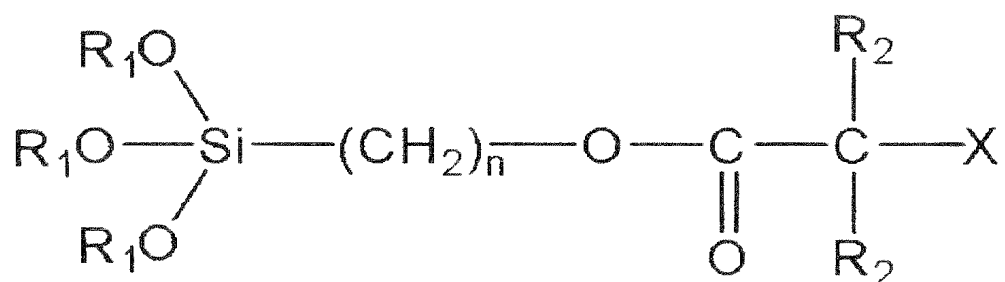
The term "phenyl group" used herein is a C₆ aromatic cyclic hydrocarbon, in other words, a functional group produced from a benzene which is deprived of one H.

In another aspect, the present invention provides a process for producing a
5 hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion, comprising the steps of:

- a) attaching a polymerization initiation group to a microparticle surface;
- b) bringing into contact a microparticle having the polymerization initiation group on its surface with a crosslinkable monomer under the conditions for living
10 radical polymerization to obtain a composite microparticle in which a high-density polymer brush layer is attached to the microparticle surface;
- c) bringing into contact a crosslinkable polymer brush of the composite microparticle with a non-crosslinkable monomer under the conditions for living radical polymerization to obtain a composite microparticle in which a block
15 copolymer is attached to the microparticle surface;
- d) subjecting the composite microparticle in which the block copolymer is attached to the microparticle surface to the conditions for crosslinking reaction; and
- e) bringing into contact the composite microparticle in which the block copolymer is attached to the microparticle surface with an eluent under such
20 conditions that the microparticle is only eluted with no influence on the block copolymer to elute only the microparticle.

In a preferred embodiment, the step a) is carried out by bringing into contact a compound represented by the formula:

[Formula 9]



and a microparticle of silica, a metal oxide or a metal sulfide under such conditions that the compound and the microparticle may react. In the formula, the spacer chain length n is preferably an integer of from 3 to 10, more preferably an integer of from 4 to 8, and most preferably 6. R_1 is preferably a C_1 to C_3 alkyl group, and more preferably a methyl group or an ethyl group. R_2 is preferably a methyl group or an ethyl group. X is preferably a halogen atom, and in particular Br.

The polymerization initiation group-containing silane coupling agents as described above can be synthesized according to the process described in Patent Literature 3. The microparticles thus obtained, having polymerization initiation group on their surfaces, are contacted with a crosslinkable monomer listed above under the conditions for living radical polymerization, to thereby obtain composite microparticles in which high-density polymer brush layers are attached to the microparticle surfaces (step b)). The crosslinkable monomer to be contacted with the microparticles having polymerization initiator substrates on their surfaces may be singular or plural in kind; however, it is preferably singular in order to obtain monodispersibility of the crosslinkable polymer brush layers.

The eluent used for the hollowing treatment (for example, step e)) is an aqueous solution of hydrogen fluoride, the concentration of which can be selected as appropriate by those skilled in the art.

During the process for producing hollow microparticles according to the present invention, an intermediate product or end product obtained at each step above can be isolated by removing foreign substances (unreacted raw materials, byproducts,

solvents, etc.) from a reaction solution by a method commonly used in the art (for example, extraction, distillation, washing, concentration, precipitation, filtration, drying, etc.) followed by an appropriate combination of post-treatment methods commonly used in the art (for example, adsorption, elution, distillation, precipitation, deposition, chromatography, etc.).

The hollow microparticles obtained according to the present invention can be confirmed by transferring a water surface film of these microparticles to a grit for transmission electron microscopes (abbreviated as TEM) to observe with a TEM. Fig. 3 shows a TEM photograph of a water surface monolayer film of hollow microparticles according to the present invention (the average particle size of the silica particles is 740 nm and the number average molecular weights of PEO and PMMA blocks composing the polymer brush layers of the hollow microparticles are 388000 and 194000 respectively). This confirmed that the hollow microparticles according to the present invention had formed a monolayer film without two-dimensional aggregation.

All references cited herein, such as scientific documents, patents and patent applications are herein incorporated by reference in their entirety to the same extent as if each reference was specifically indicated to be incorporated by reference.

As so far described, the present invention has been described using the preferred embodiments thereof, but it should not be limited to such embodiments. It is recognized that the scope of the invention is limited only by the claims. It is understood that those skilled in the art, reading the description of specific preferred embodiments of the invention, can work equivalent scopes in the light of the description of the invention and technical common knowledge. It is to be understood that all patents, patent applications and literatures cited herein are herein incorporated by reference in their contents to the same manner as if they were specifically indicated to be incorporated by reference.

EXAMPLES

(Example 1: Introduction of initiation group to silica microparticle surfaces)

A dispersion of silica microparticles (Nippon Shokubai, average particle size 740 nm) in ethanol (7.7% by weight, 30 mL) was added to a mixed solution of 28% aqueous ammonia solution (13.9 g) and ethanol (200 mL). After agitating the solution at 40°C for two hours, 6-(2-bromo-2-methylpropionyloxy)hexyltriethoxysilane (2 g) dissolved in ethanol (10 mL) was added dropwise and agitation was carried out at 40°C for 18 hours. Thereafter, silica microparticles were recovered by a centrifuge, washed with ethanol and anisole and then stored in anisole.

(Example 2: Preparation of hollow microparticles)

Hollow microparticles were synthesized according to the procedure as follows (Fig. 1). To the dispersion of silica microparticles having polymerization initiation group in anisole (4 g) prepared in Example 1, 3-ethyl-3-methacryloyloxy-methyloxetane (EMO, 10 g) and, as a free initiator, ethyl 2-bromoisobutyrate (EBIB, 3.5 mg) were mixed and dissolved gas was replaced with argon. To this mixture, a solution, previously replaced with argon, of Cu (I) Br (13 mg)/4,4'-dinonyl-2,2'-dipyridyl (dNbipy, 74 mg) complex in anisole (6g) was added in a glove box and, after hermetically sealing, polymerization was carried out in a temperature-controlled shaking bath at 60°C for 24 hours. The obtained poly(EMO)(PEMO)-grafted silica microparticles (PEMO-SiP) were washed with acetone to remove free polymers grown from the free initiator. Next, PEMO-SiP (0.4 g) was mixed with methyl methacrylate (MMA, 40 g) and EBIB (13 mg) and dissolved gas was replaced with argon. To this mixture, Cu (I) Br (66 mg)/dNbipy (545 mg) complex in anisole previously replaced with argon was added in a glove box and, after hermetically sealing, polymerization was carried out in a temperature-controlled shaking bath at 70°C for ten hours. The grafted silica microparticles were washed with acetone to remove free polymers grown from the free initiator, to thereby synthesize silica

microparticles grafted with a block copolymer (PEMO—b—PMMA) consisting of PEMO and poly(MMA)(PMMA). The block copolymer-grafted silica microparticles (0.2 g) were dispersed in dichloromethane (10 g) and dissolved gas was replaced with argon. This dispersion was transferred to a glove box, $\text{BF}_3 \cdot \text{OEt}_2$ (0.1 g) as a ring-opening reaction initiator was added and agitation was carried out at room temperature for 18 hours. The microparticles were washed with toluene and recovered as a dispersion in toluene. To this dispersion in toluene (0.4% by weight, 50 g), hydrogen fluoride (HF) diluted with water (10% by weight, 50 g) and, as a phase transfer catalyst, tri-n-octylmethylammonium chloride (0.5 g) were added and vigorous agitation was carried out for 15 hours to elute silica microparticles. After washing the toluene phase with aqueous hydrogen bicarbonate solution and then with water, hollow microparticles were recovered by a centrifuge.

The number average molecular weights of PEMO and PMMA blocks of the block copolymer grafted to the silica microparticle surfaces were 388000 and 194000 respectively, and the molecular weight distribution indices were 1.21 and 1.40 respectively. Infrared absorption spectra of the microparticles before BF_3 treatment, after BF_3 treatment and after HF treatment are shown in Fig. 2. After BF_3 treatment, the peak derived from an oxetane ring (990 cm^{-1}) decreased, indicating that oxetane ring-opening reaction had facilitated the crosslinking reaction of the PEMO blocks. After HF treatment, the peak derived from Si-O (1100 cm^{-1}) disappeared, indicating that the silica microparticles had been eluted. A transmission electron micrograph of the microparticles after HF treatment is shown in Fig. 3. The color at the center of each microparticle appears pale, confirming a hollow shape. As a result of dynamic light scattering determination of microparticles before crosslinking and hollow microparticles, their particles sizes and standard deviations are approximately the same in value, indicating that the microparticles retain high dispersibility without aggregation during the process of preparing the hollow microparticles. This is

supposedly due to that the PEMO and PMMA blocks were separated by high distensibility inherent to the high-density polymer brushes, with the PMMA blocks acting as protective layers for preventing crosslinking between the microparticles.

INDUSTRIAL APPLICABILITY

5 According to the processes for producing hollow microparticles of the present invention, hollow particles, while retaining characteristics of prior art, high-density polymer particles of having a narrow particle size distribution and an excellent dispersion stability, can be obtained. Also, any hollow microparticles may be obtained by the selection of particle shape and size. In addition, by adjusting the
10 degree of crosslinking and the like of the crosslinkable polymer for the inner layer, shape-retaining characteristics (rigid or flexible) of the hollow portion may be controlled and, when the hollow portion is to carry or take in a reagent and agent, their sustained release rate and/or intake rate can also be controlled. Furthermore, particle sizes can arbitrarily be designed by controlling the film thickness of the high-
15 density grafted chains at the outer side.

The hollow microparticles provided by the present invention have applicability in the fields or as the products enumerated below:

- 1) Microparticles whose functions rely on macromolecular materials (for example, biodegradable particles, etc.)
- 20 2) Microparticles whose surfaces control functions (for example, affinity particles, adsorbents, scatterers, catalysts, etc.)
- 3) Microparticles whose functions can be controlled by inclusions (quantum dots, fluorophores, pigments, dyestuff, drugs, magnetic substances, CMP (chemical mechanical polishing) abrasives, microreactors, heat insulators, etc.)
- 25 4) Microparticles whose functions are provided by regularity of arrangement (photonic crystals, diffraction gratings, light modulating devices, electronic papers, materials for waveguides)

- 5) Microparticles for providing dynamic functions (particle pumps, etc.)

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 illustrates an example of synthesis procedure of hollow microparticles according to the present invention.

- 5 Fig. 2 shows infrared absorption spectra for a microparticle grafted with a block copolymer (PEMO—b—PMMA) according to the process of the present invention, before BF_3 treatment, after BF_3 treatment and after HF treatment.

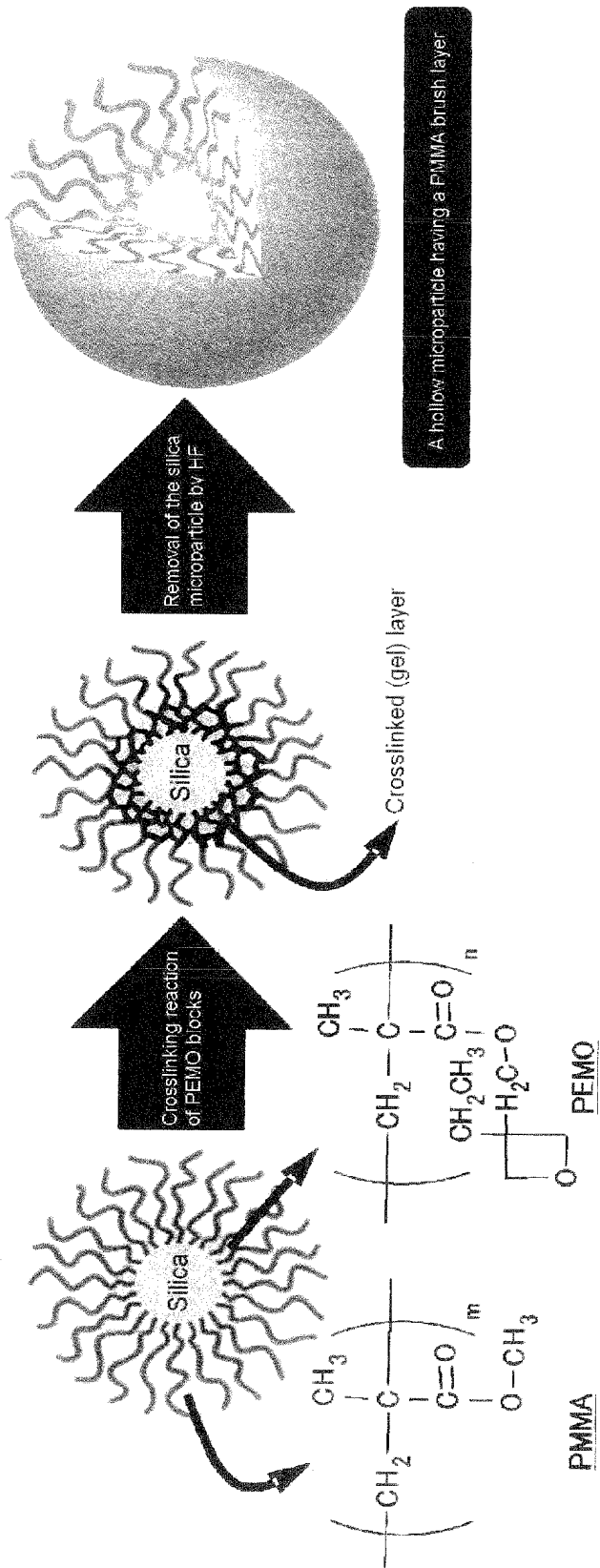
Fig. 3 is a transmission electron micrograph of a water surface monolayer film of hollow microparticles according to the present invention.

ABSTRACT

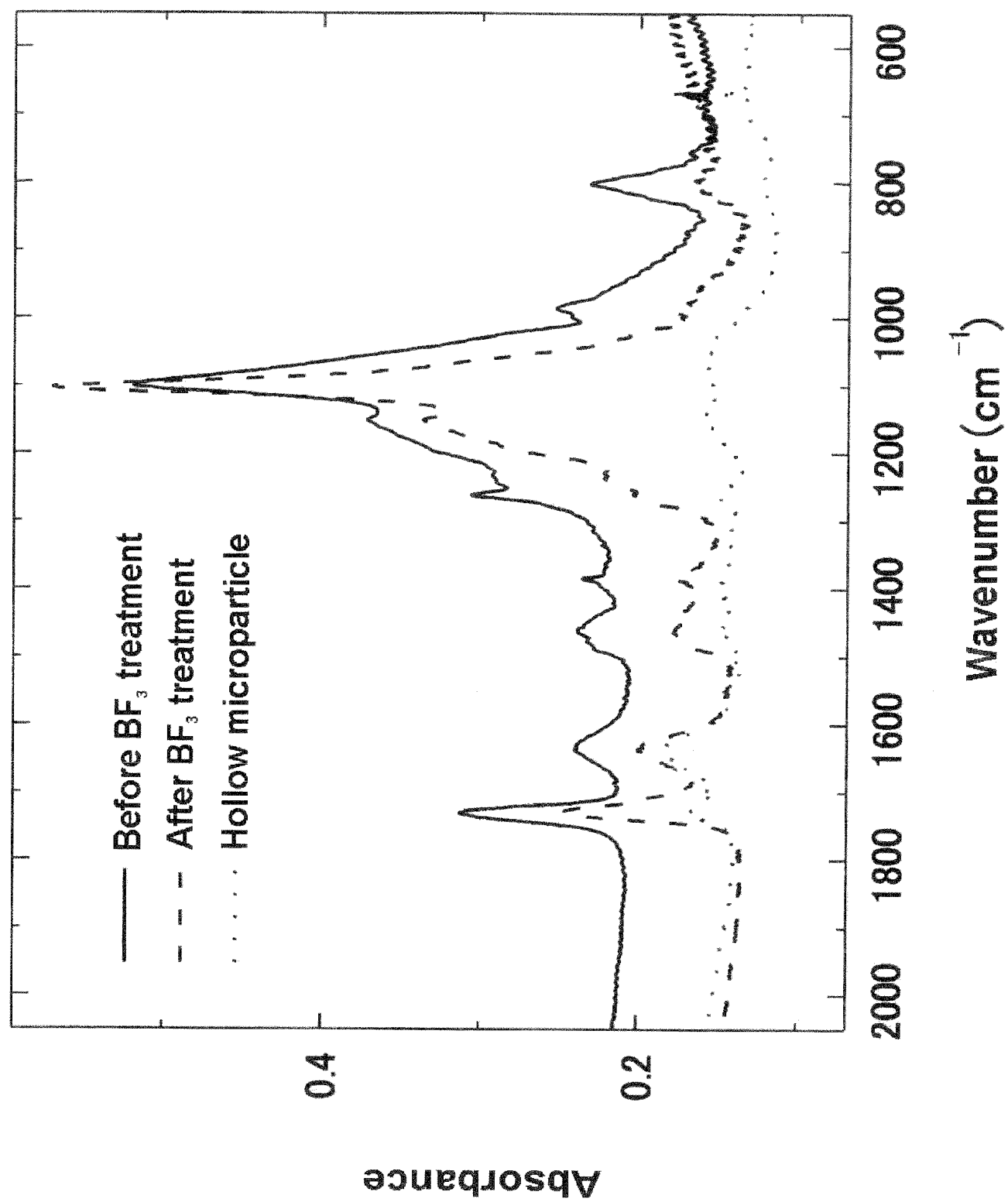
The object of the present invention is to provide a process for hollowing a composite microparticle made of high-density grafted chains attached to a microparticle surface without compromising characteristics of prior art, high-density polymer particles of having a narrow particle size distribution and an excellent dispersion stability and to provide, by such a process, a hollow microparticle comprising a high-density polymer brush layer and a hollow portion.

The present inventions provides a process for hollowing a microparticle, by eluting only a microparticle from a composite microparticle made of high-density grafted chains attached to a microparticle surface and provides, by such a process, a hollow microparticle comprising a hollow portion and a high-density polymer brush layer enclosing the hollow portion.

[Fig. 1]



[Fig.2]



[Fig.3]

